Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 2-4, 6, 12, 13 and 15-18 are pending in the application. Claims 1, 5, 7, 8, 11 and 14 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. Applicant reserves the right to file a divisional application directed to the subject matter of canceled claims 1, 5, 7, 8, 11 and 14. New claims 15-18 are sought to be added. Support for these claims can be found throughout the specification as filed, as detailed below. These claims are believed to introduce no new matter, and their entry is respectfully requested.

Claim 2 is sought to be amended. The preamble has been amended to make explicit the context for performing the claimed method. The steps for performing the simulation of the claimed method have also been made explicit. Claims 3, 4, 6 and 13 are sought to be amended similarly. Claim 12 is sought to be amended to conform its language to that of amended claim 2. Support for these changes can be found throughout the specification as filed, as detailed below. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Support for claims 2, 3 and 4 is found, *inter alia*, in original claims 2, 3 and 4, respectively; and in the specification, at page 7, lines 3-11, 14-16 and 21-24, and at page 9, lines 16-19 and page 10, line 4 through page 11, line 1, in combination with the following: page 6, lines 17-19 (definition of organic fragment); page 17, lines 16-18 (definition of *B*); page 14, line 12 through page 16, line 23 (determination of acceptance or rejection); and page 5, lines 25-26 (definition of cluster). Support for claims 6 and 15 is found, *inter alia*,

in original claim 6; and in the specification, as described for claims 2-4, above, and at page 3, lines 6-11 and page 11, lines 11-13 and 20-22. Support for claim 12 is found, *inter alia*, in original claim 12; and in the specification, at page 6, lines 17-19. Support for claims 13 and 16 is found, *inter alia*, in the specification, as described for claim 3, above; and at page 11, line 23 through page 12, line 13. Support for claim 17 is found, *inter alia*, in the specification, at page 7, lines 12-16. Support for claim 18 is found, *inter alia*, in the specification, at page 7, lines 16-19.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Restriction Requirement

The Examiner withdrew unelected claim 8 from consideration and requested cancellation thereof. Solely to expedite prosecution of the above-captioned application, Applicant has canceled claim 8.

Objection to the Specification

The specification is objected to as addressing various sources of information identified only with "as submitted." Specifically, these sources are the crystal solutions of Mattos *et al.*, at page 12, lines 25, 26-27, 27-28, 29-30 and 30-31, and of Ding *et al.*, at page 12, line 32. Applicant has amended the specification to better identify these sources of this information and to correct one typographical error. Reconsideration and withdrawal of the objection to the specification is respectfully requested.

In copending divisional application no. 09/722,731, containing a specification identical to that of the above-captioned application, the Examiner requested that Applicant remove the list of references and the numerical numbering of references from the specification. The list of references, at page 21, lines 14-24, has been deleted from the captioned application as well. Applicant has deleted the numerical superscripts and inserted the corresponding references therefor. No new matter has been added. It is readily apparent that the superscript "7" on page 19, line 8 was a typographical error, and that it should have referred to the reference numbered "8". This is apparent because there is no nominal citation to reference no. 8 anywhere in the specification, the literal reading of which would render the inclusion of reference no. 8 superfluous. Thus, the replacement of the noted superscript "7" with reference no. 8 does not constitute the addition of new matter. Additionally, a grammatical error has been corrected in the paragraph beginning on page 19, line 6, which correction does not constitute the addition of new matter.

Drawings

The Examiner did not object to the drawings. However, in copending divisional application no. 09/722,731, containing drawings identical to those of the above-captioned application, the Examiner objected to the drawings under 37 C.F.R. § 1.84(g) and (l). Applicant submits herewith a petition under 37 C.F.R. § 1.84(a)(2) to accept color drawings in the captioned application. The color drawings are believed to comply with the relevant rules. The specification has been amended to comply with 37 C.F.R. § 1.84(a)(2)(iv).

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-7 and 11-14 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that the Applicant regards as the invention. Applicant respectfully traverses. Each of the Examiner's rejections, labeled A-K, is addressed, either alone or with sufficiently similar or related rejections as to justify common treatment.

The Examiner asserts that "Parameter *B*" must be defined and that the steps involved in the "simulated annealing of chemical potential calculations" must be provided in the claims (rejection A); that it is not clear whether values of "Parameter *B*" refer to macromolecule, organic fragment, and/or both (rejection B); and that it is not clear whether two or more simulated annealings are conducted for each separate value of parameter *B* or whether one annealing is conducted at each "*B*" value (rejection C). Applicant traverses for at least the following reason.

Parameter *B* is described in the specification at, for example, page 14, line 26 through page 15, line 21. Furthermore, the specification describes Parameter *B* with reference to organic fragments. Accordingly, amended claim 2 recites Parameter *B* as $\mu'/kT + ln\langle N\rangle$, where μ' is the excess chemical potential, k is Boltzmann's constant, T is the absolute temperature, and $\langle N\rangle$ is the mean number of molecules of the molecule or molecular fragment. The amended claim further recites that steps (1)-(4) are performed at a single value of *B*; then a lesser value of *B* is chosen at which to repeat steps (1)-(4). *See* claim 2, step (5). Therefore, Applicant respectfully submits that Parameter *B* and features related thereto are not indefinite. The same arguments apply to amended claim 6, and to claims that

depend from claim 2 or claim 6. Reconsideration and withdrawal of these rejections under 35 U.S.C. § 112, second paragraph is respectfully requested.

The Examiner asserts that in claim 6 it is not clear whether steps (e)-(g) are made in addition to or in the alternative to steps (a) and (b) of claim 1 (rejection I). Applicant respectfully traverses. Amended claim 6 is written in independent claim form comprising a series of discrete steps. The claim specifies which steps are to be performed using an organic fragment, which are to be performed using water, and how the overall output is to accommodate the output of each operation. Thus, Applicant submits that there is no ambiguity about which steps the claim encompasses. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

Applicant respectfully submits that the remaining rejections are overcome by the language of the amended claims. Specifically, the following rejections are directed to language that does not appear in the amended claims: D. (which "solutions", and "converged" via which steps, are used to identify "first locations"; and which one out of the plurality of ORFs is the "relevant ORF" used to identify "first locations"); E. ("strongly bound"); F. (which method steps are involved in "reducing the binding stringency"); G. (which "elements" are being identified; meaning of "contribute to the binding"); H. (which "bioactive agent" is addressed in the claim); J. (which "ligand molecules" are addressed); and K. ("strongly bound"). Reconsideration and withdrawal of these rejections under 35 U.S.C. § 112, second paragraph is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 2-5 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabling for a plurality of organic fragments or for further identifications of elements contributing to the binding of biological agents. The Examiner asserts that the method steps achieving such determinations are neither illustrated in the form of working examples nor addressed in the form of explicit guidance. Applicant traverses for at least the following reasons.

The method according to amended claim 2 recites a (*i.e.*, at least one) molecule or molecular fragment. The Examiner conceded that the specification is "enabling for determining of [sic] binding sites for one ORF (or water)." Applicant submits that amended claims 3 and 4 (and new claim 15), which recite more than one organic molecule or molecular fragment, provide explicit guidance in implementing the methods claimed therein. Each of these claims specifies precisely which of the enumerated steps are to be repeated for each molecule or molecular fragment, and specifies how to adjust the output to accommodate the additional information that is generated by the additional steps. The use of the method for multiple organic fragments is described, *inter alia*, in the specification, at page 9, lines 16-19, and at page 10, line 4 through page 11, line 1. As the cited portion of the specification teaches, the same steps performed with one molecule or molecular fragment can be performed with other molecules or molecular fragments. The clusters are then identified from the combined results of the individual simulations. *See* page 9, lines 12-16, and page 5, lines 25-26.

Similarly, Applicant submits that amended claim 13 (and new claim 16) provides specific guidance in implementing the method claimed therein. This claim specifies

precisely which of the enumerated steps are to be repeated for each molecule or molecular fragment and the simulation conditions under which these steps are to be performed, and specifies the output to be generated by the additional steps. With the portions of the specification cited in the preceding paragraph, the specification at page 11, line 23 through page 12, line 13 teaches the use of the method to identify sites in the vicinity of clusters that more weakly bind molecules or molecular fragments. Specifically, the more weakly binding molecules or molecular fragments are those that appear in the simulation at less than the highest affinity value. The affinity value for the unrejected instances of a molecule or molecular fragment is larger when the simulation is run at a lower *B* value. *See, e.g.*, page 9, lines 3-11. Thus, outputting the unrejected instances of a molecule or molecular fragment for a simulation conducted at a higher value of *B* reveals the more weakly binding molecules or molecular fragments. In view of the preceding, Applicant submits that amended claims 2-4 and 13 are fully enabled. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 6 and 14 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Guarnieri and Mezei, *J. Am. Chem. Soc. 118*:8493-8494 (1996) ("Guarnieri"). The Examiner asserts that Guarnieri teaches a method of identifying binding sites of water using the method of simulated annealing of chemical potential calculations with water as the inserted solvent. Further, the Examiner asserts that the calculations are carried out at several values of parameter *B*. Applicant traverses for at least the following reason.

The Guarnieri method purportedly reveals the locations of solvation of a biomolecule. However, locations of solvation, *i.e.*, locations at which water is strongly bound, are *not* candidate sites for binding ligands. *See* specification, at page 3, lines 8-11. The method of Guarnieri samples potential hydration positions around the molecule by inserting and deleting *water molecules* from the simulation cell. *See* Guarnieri, at 8493, ¶ 2, lines 4-6. The context of the reference is the crucial role that water plays in DNA and protein architecture and in many DNA and protein functions. *See id.* at ¶ 1. There is no mention of candidate sites for binding molecules or fragments other than water.

In contrast, amended claim 6 comprises a series of steps performed with a molecule or molecular fragment *other than water*. *See* claim 6, the line between steps (5) and (6). The preceding paragraph makes clear the crucial difference between water-binding sites and sites at which organic molecules or organic fragments bind. This difference is captured in step (7), for example, in which the output comprises a list of the unrejected instances of the organic molecule or organic molecular fragment that are *not* associated with unrejected instances of the water molecule. Guarnieri does not teach implementing the method of claim 6 using an organic molecule or organic fragment. Thus, Applicant respectfully submits that Guarnieri fails to teach all of the recited elements of amended claim 6. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1-5, 7 and 11-13 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Guarnieri and Mezei, *J. Am. Chem. Soc. 118*:8493-94 (1996) ("Guarnieri"), in view of Resat, H. and Mezei, M., *Biophys. J. 71*:1179-90 (1996) ("Resat"), or Morgantini, P.-Y. and Kollman, P.A., *J. Am. Chem. Soc. 117*:6057-63 (1995) ("Morgantini"), or Blaskó, A. *et al.*, *J. Org. Chem. 58*:5738-47 (1993) ("Blaskó"), or Siepmann, J.I. and McDonald, I.R., *Molec. Phys. 79*:457-73 (1993) ("Siepmann"), or Koone, N. *et al.*, *J. Phys. Chem. 99*:16976-81 (1995) ("Koone"), or Gibson, K.D. and Scheraga, H.A., *J. Phys. Chem. 99*:3765-73 (1995) ("Gibson"), or Brandmeier, V. *et al.*, *Helv. Chim. Acta 77*:70-85 (1994) ("Brandmeier"), or Johnson, P.M., in *Resonance Ionization Spectroscopy*:145-50 (1990) ("Johnson"), or Basson, I. and Reynhardt, E.C., *J. Phys. D: Appl. Phys. 21*:1434-37 (1988) ("Basson"), or Ranieri, F.O. *et al.*, *Chem. Phys. 183*:187-205 (1994) ("Raineri"), or Mokrosz, J.L. *et al.*, *J. Het. Chem. 33*:1207-10 (1996) ("Mokrosz"), or Duggan, B.M and Craik, D.J., *J. Med. Chem. 39*:4007-16 (1996) ("Duggan"), or Clough, S.B. *et al.*, *Macromolecules 26*:597-600 (1993) ("Clough"), or Lunazzi, L. *et al.*, *J. Org. Chem. 62*:2263-2266 (1997) ("Lunazzi"), or Lee, T. and Jones, J.B., *J. Am. Chem. Soc. 118*:502-508 (1996) ("Lee").

The Examiner asserts that Guarnieri teaches a method of identifying binding sites of water using a method of simulated annealing of chemical potential calculations using water as the inserted solvent, but does not teach calculating binding sites for organic fragments. The Examiner further asserts that Resat, Morgantini, Blaskó, Siepmann, Koone, Gibson, Brandmeier, Johnson, Basson, Ranieri, Mokrosz, Duggan, Clough, Lunazzi and Lee collectively demonstrate the utility of applying molecular dynamics studies to various "organic fragments." Thus, the Examiner concludes it would have been obvious to one

skilled in the art at the time the invention was made to be motivated to apply the method of Guarnieri of identifying hydration sites on a macromolecule to determine binding sites for any compounds of interest. Applicant respectfully traverses for at least the following reason.

The Examiner asserts that the above references demonstrate the *utility* of applying "molecular dynamics" studies to various organic fragments. Assuming *arguendo* that the Examiner is correct, which the Applicant does not concede, such a demonstration of utility is not sufficient to establish a *prima facie* case of obviousness under 35 U.S.C. § 103. To establish a *prima facie* case of obviousness, (i) there must be some suggestion or motivation to modify the reference or to combine reference teachings, (ii) there must be a reasonable expectation of success, and (iii) the reference(s) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Guarnieri purportedly reveals the locations of solvation of a biomolecule, and it does so in the context of examining the crucial role that water plays in DNA and protein architecture. *See* Guarnieiri, at 8493, ¶ 1. The Guarnieri method samples potential hydration positions around the molecule by inserting and deleting water molecules from the simulation cell. *Id.* at ¶ 2, lines 4-6. The Examiner concedes that the reference does not teach determining binding sites for organic fragments, but asserts that motivation existed at the time of invention to apply Guarnieri's method for any compounds of interest, such as those described in the cited references. Each of these references is taken in turn.

Resat recites that "perhaps the most challenging part of the structure refinement process is the determination of the locations and the number of solvating water molecules," and it states that "the object of [the] study is to determine what are the likely locations for the solvating waters in the dCpG/proflavine crystal hydrate by using the [cavity-biased grand

canonical Monte Carlo] method." Resat, at 1180, ¶ 3, and 1182, ¶ 2. The context of these statements is Resat's assertion that solvation effects can have a significant influence on properties of biomolecules. *Id.* at 1180, ¶ 1. In Resat there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Morgantini purportedly performs calculations using an empirical potential energy function to determine aqueous solvation free energies of ammonia, several acetamides and several amines. Morgantini, at 6057, ¶¶ 4-5. In Morgantini there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Blaskó states that "[a] convenient way to study dynamic properties in solution is by quantifying the segmental motions in the molecule using ^{13}C spin-lattice relaxation times (T_1)." Blaskó, at 5738, ¶ 3. The stated purpose of the experiment described therein was to determine the solution structure of a phenol pendant-capped porphyrin and its iron(III) complex. *Id.* at ¶ 4. In Blaskó there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated purpose of the simulations described in Siepmann was to investigate the microscopic structure of a self-assembled monolayer of hexadecyl mercaptan chemisorbed on ^{111}Au. Siepmann, at 458, ¶ 2. The configurational-bias Monte Carlo scheme was used to sample the conformations of the chains, the method of Barker and Watts was used for the rotations, and translational moves were performed in "the standard way". *Id.* at 460, ¶ 2. In Siepmann there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated purpose of the experiments described in Koone was to discuss the motion of solvent molecules in small geometries, namely, to conduct experimental work in order to

provide a satisfactory theory for diffusion within the confined geometry of porous glass having average pore diameters of less than 4.0 nm. Koone, at 16976, ¶ 3. Experimental results obtained for cyclohexane and toluene were purportedly compared with molecular dynamics computer simulations data. *See id.* at 16977, ¶ 1 and 16980, ¶ 3. In Koone there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Gibson purportedly describes the application of a potential to study the possible ways of packing benzene in a crystal by energy minimization from different starting points. Gibson, at 3765, ¶ 4. Secant-type unconstrained minimization solver with rescaling was used to minimize the energy. *Id.* at 3766, last ¶ and references therein. In Gibson there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Brandmeier purptedly describes the synthesis and conformational study of biphenyl-containing cyclic peptides. Brandmeier, at 71, ¶ 1. A molecular dynamics study was performed, using the GROMOS-program package for the MD calculations, to obtain a survey of the conformational space that can be reached by one of the peptides of interest. *Id.* at 77, ¶ 3. Brandmeier suggests that the data discussed therein may serve as a guide for the design of synthetic biphenyl compounds with peptide conformations fixed in a β-sheet arrangement. *Id.* at 82, ¶ 2. In Brandmeier there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Johnson purportedly examines the multiphoton ionization process to glean information about the dynamics of resonant intermediate states of carbon dioxide and pyrazine. *See* Johnson, at 145, abstract, and 150, ¶ 2. Analyzing photoelectron or field

ionization spectra, the investigators were able to follow processes ranging from photodissociation to internal energy rearrangement. *Id.* at 150, ¶ 2. In Johnson there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Basson purportedly describes an investigation of the structure and molecular dynamics of montan wax by means of x-ray powder diffraction, differential scanning calorimetry and wide-line NMR. Basson, at 1434, ¶ 2. The "molecular dynamics" aspect of the reference consists of investigations of laboratory frame spin-lattice relaxation, spin-spin relaxation, and spin-lattice relaxation in the rotating frame, including correlations to the reorientational-translational motion of the chains. *Id.* at 1436, last ¶ through 1437, ¶ 5. In Basson there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated purpose of the work described in Raineri was to generalize a previously described molecular theory of the solvation time correlation function to resolve the spatial and temporal dependence of the solvation response. Rainieri, at 188, ¶ 3. The investigators' theory of solvation dynamics is based on the premise that accurate results for the solvent response may be derived from an approximate treatment of the dynamical problem cast in terms of a *surrogate* time-dependent Hamiltonian in which the solute-solvent coupling is expressed in terms of *renormalized* interactions. *Id.* at ¶ 5. In Raineri there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Mokrosz purportedly reports conformational studies of substituted heteroarylpyrimidines performed using ^{1}H NMR and molecular modeling methods. *See* Mokrosz, at 1207, ¶ 1. The investigators' NMR experiments suggested that 4-(2-furyl)-

2-methylaminopyrimidine exists in acetone-d6 at low temperature as an equimolar mixture of conformers and that it adopts an *s-trans* orientation. *Id.* at 1207, ¶ 2 and 1208, ¶ 1. Molecular modeling studies were performed using the PM3 and molecular dynamics approaches in order to verify the results of the conformational analysis. *Id.* at 1208, ¶ 4. In Mokrosz there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

Duggan purportedly measures NMR spin-lattice relaxation times and nuclear Overhauser enhancement factors in order to have an understanding of the internal molecular dynamics of various thyroid hormones. Duggan, at 4007, ¶ 1. The stated interest is in the internal molecular motion in bioactive species as a knowledge of the rate and amplitude of motions in solution places limits on conformations that may be expected in the bound state. *Id.* at 4008, ¶ 3. The sole mention of binding to macromolecules is as follows: "The fact that thyroxine and other thyroid hormones are able to so freely move over a moderately large region of conformational space has implications for receptor binding. . . . The conformational flexibility shown by the thyroid hormones may be required for binding." *Id.* at 4015, ¶ 1. In Duggan there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated interest of Clough is in a family of substituted polyacetylenes displaying high degrees of conjugation, including extensively conjugated backbones, and possessing high charge densities, in contrast to typical substituted polyacetylenes. *See* Clough, at 597, ¶¶ 1,3. Modeling studies were undertaken to determine the structural characteristics responsible for the unique properties of these substituted polyacetylenes. *Id.* at ¶¶ 4,5. Molecular mechanics and molecular dynamics calculations yielded information relating to

charge distribution and chain conformation. *See id.* at 598, ¶ 6 through 600, ¶ 2. In Clough there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated interest of Lunazzi is in the kinetic stabilization of thioaldehydes via steric hindrance, specifically via restricted rotation about the sp^2-sp^2 carbon-carbon bond in aryl or vinyl thioaldehydes. *See* Lunazzi, at 2263, ¶ 1. Thus, Lunazzi investigates the carbon-carbon rotational barrier about the Ar-CHS bond in several aryl aldehydes using NMR. *See id.*, passim. The only mention of molecular mechanics is in reference to predicting the relative dipole moments of *E* and *Z* rotamers of 3-amino-furan-2-thiocarbaldehyde. *Id.* at 2263, ¶ 5. In Lunazzi there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The stated interest of Lee is in identifying and understanding the factors controlling enzyme substrate and inhibitor binding, particularly with respect to remote stereocontrol in catalysis. *See* Lee, at 502, ¶ 1. For the two serine proteases used in the study, the active site is *known*. *See id.* at ¶ 2. Furthermore, aldehydes are used as inhibitors because aldehydes are known to be transition state analog competitive inhibitors of serine proteases. *Id.* at 503, ¶ 2. Kinetic data was obtained, and "[m]olecular modeling was applied in order to interpret the kinetic data more completely." *Id.* at 504, ¶ 3. The modeling was used to determine the conformations of bound substrate. *See id.* at 504, ¶ 3 through 505, ¶ 1. Although the binding of an organic molecule to a macromolecule is discussed, as mentioned, the binding sites of the enzymes studied were known. In Lee there is no mention of, much less any suggestion of, analyzing a macromolecule for potential binding sites.

The Examiner's argument neglects to make any distinction between different computational methods—simply labeling them all as "molecular dynamics"—or any distinction between the claimed method, which relates to analyzing a macromolecule for potential binding sites for a molecule or molecular fragment, and the methods reported in the above references. Applicant respectfully submits that when these distinctions are properly borne in mind, a *prima facie* case of obviousness has not been established for at least the reason that there is no suggestion or motivation to modify the teachings of Guarnieri to arrive at the claimed invention, or to combine the teachings of Guarnieri with any of the cited references and subsequently modify them to arrive at the claimed invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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